Patent
Attorney's Docket No. 1024637-000191

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of	**Mail Stop: APPEAL BRIEF - PATENTS**
Peter KITE et al.	
Application No.: 10/659,413	Group Art Unit: 1617
Filed: September 10, 2003	Examiner: Shobha Kantamneni
For: ANTISEPTIC COMPOSITIONS, METHODS AND SYSTEMS	Confirmation No.: 4621
	Appeal No.: 1

APPEAL BRIEF

Mail Stop APPEAL BRIEF - PATENTS
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This appeal is from the decision of the Office issued on February 24, 2006, finally rejecting claims 32, 34, 37, 39, 41, 42, 45-47 and 55-60, which are reproduced as the Claims Appendix of this brief.

☒ A check covering the ☐ $250.00 (2402) ☒ $500.00 (1402) Government fee is filed herewith.

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The Commissioner is hereby authorized to charge any appropriate fees under 37 C.F.R. §§1.16, 1.17, and 1.21 that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800.

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I. Real Party in Interest

The present application is assigned to Tyco Healthcare Group LP which is the real party in interest.

II. Related Appeals and Interferences

Appellants' legal representative and assignee are aware of one other appeal or interferences which may affect or be directly affected by or have a bearing on the Board's decision in the pending appeal. The Board is directed to an Appeal and associated Appeal Brief for U.S. Patent Application Serial No. 10/313,844. A Related Proceedings Appendix is attached.

III. Status of Claims

Claims 32, 34, 37, 39, 41, 42, 45-47 and 55-60 are pending, rejected and presently appealed. A copy of the claims involved in the appeal is contained in an attached Claims Appendix.

IV. Status of Amendments

No amendments have been filed subsequent to the final rejection of February 24, 2006.

V. Summary of Claimed Subject Matter

The claimed subject matter involves antiseptic solutions comprising at least one salt of ethylene diamine tetraacetic acid (EDTA) in solution, wherein the at least one EDTA salt comprises at least one of tri-sodium and tetra-sodium EDTA at a prescribed concentration and/or pH. The inventors have discovered, unexpectedly, that certain EDTA compositions provide powerful antiseptic activities and function as broad-spectrum anti-microbial agents, as well as fungicidal agents against many strains of pathogenic yeast. EDTA compositions of the claimed subject matter are also highly effective in killing pathogenic biofilm organisms and in reducing and eliminating existing biofilms, as well as preventing biofilm formation. EDTA compositions moreover exhibit anti-protozoan activity including anti-amoebic activity. *See, e.g.,* specification page 8, lines 16-24. They are thus highly effective antiseptic compositions.

Because the EDTA compositions of the claimed subject matter have the wide spectrum antiseptic activities described above, and because they are safe for human administration and are biocompatible and non-corrosive, they have numerous applications, including applications as lock and lock flush solutions for various types of catheters, use as antiseptic agents or solutions for sanitizing a range of medical, dental and veterinary devices, instruments and other objects, surfaces, and the like. *See, e.g.,* specification page 8, lines 27-34.

The efficacy of the claimed compositions is superior to many antiseptic compositions conventionally used for these applications. The claimed compositions are additionally effective in preventing biofilm formation and substantially eliminating biofilm organisms, which many antibiotics and biocidal agents are not. The claimed compositions do *not* contribute to antibiotic resistance, which provides yet another important benefit.

Four of the appealed claims are in independent format: claims 32, 55, 56 and 57. Independent claim 32 recites an antiseptic composition comprising at least one of tri-sodium and tetra-sodium EDTA in solution at a concentration of at least 2.0% (w/v) and less than 15% (w/v) and having a pH of at least 9.5, wherein the antiseptic composition has a bactericidal effect over a broad spectrum of microbes and is packaged in a sterile, non-pyrogenic form. Independent claim 55 additionally recites that the solution is water and the antiseptic composition has an osmolarity of from 240-500 mOsM/Kg. Independent claim 57 recites an antiseptic composition comprising tri- and tetra-sodium EDTA in solution at a concentration sufficient to have antimicrobial activity and at a pH of at least 9.5, wherein the antiseptic composition has a bactericidal effect over a broad spectrum of microbes and is packaged in a sterile, non-pyrogenic form. Independent claim 56 recites a lock flush composition comprising at least one of tri-sodium and tetra-sodium EDTA in solution at a concentration of at least 2.0% (w/v) and less than 15% (w/v) and having a pH of at least 9.5, wherein the antiseptic composition is packaged in a sterile, non-pyrogenic form and is biocompatible for use in in-dwelling access catheters, urinary catheters, nasal tubes and throat tubes.

Appellants' claimed antiseptic compositions and lock flush compositions are provided in a sterile and non-pyrogenic form and may be packaged in any convenient fashion. In some embodiments, antiseptic EDTA compositions of the

claimed subject matter may be provided in connection with or as part of a medical device, such as in a pre-filled syringe (Claim 46) or in a single dose vial (Claim 47). The compositions may be prepared under sterile, aseptic conditions, or they may be sterilized following preparation and/or packaging using any of a variety of suitable sterilization techniques.

The claimed compositions may be provided in a saline solution (claim 39), as well as in a solution comprising less than 10% (v/v) ethanol and water (claim 37). According to further embodiments of appellants' claimed compositions, the EDTA salt, or the combination of tri-sodium and tetra-sodium EDTA salt provides at least 50% of a total antimicrobial activity of the composition (claims 58 and 59, respectively).

VI. Grounds of Rejection to be Reviewed on Appeal

1) Claims 32, 34, 39, 41, 42, 45 and 55-60 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Fahim (WO 00/13656) in view of Wider (U.S. Patent No. 6,500,861).
2) Claim 47 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Fahim (WO 00/13656) in view of Wider (U.S. Patent No. 6,500,861) and further in view of *Root et al* ("Inhibitory Effect of Disodium EDTA upon the Growth of *Staphylococcus epidermidis* In Vitro: Relation to Infection Prophylaxis of Hickman Catheters").
3) Claim 46 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Fahim (WO 00/13656) in view of Wider (U.S. Patent No. 6,500,861) and further in view of Remington's Pharmaceutical Sciences.
4) Claims 32, 34, 37, 41, 42, 45 and 55-60 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Kurginski (GB 1 279 148) in view of Fahim (WO 00/13656) and Wider (U.S. Patent No. 6,500,861).

VII. Argument

1) § 103(a) – Fahim in view of Wider

Independent claims 32, 55, 56 and 57 and pending dependent claims 34, 39, 41, 42, 45, and 58-60 are finally rejected under 35 U.S.C. § 103(a) as being unpatentable over Fahim (WO 00/13656) in view of Wider (U.S. Patent No.

6,500,861). Appellants submit that the Examiner has not established a *prima facie* case of obviousness and this rejection must therefore be withdrawn.

Claims 32, 34, 39, 41, 42, 45, 55, 57 and 60

Claims 32, 34, 39, 41, 42, 45, 55, 57 and 60 are argued as a group with respect to patentability in view of the final rejection. Independent claim 57 recites antiseptic compositions comprising tri- and tetra-sodium EDTA in solution at a concentration sufficient to have antimicrobial activity, wherein the composition has a bactericidal effect over a broad spectrum of microbes, has a pH of at least 9.5, and is packaged in a sterile, non-pyrogenic form. Independent claims 32 and 55 recite similar subject matter and specify a concentration of at least 2.0% (w/v) and less than 15% (w/v) of an EDTA salt (at least one of tri- and tetra-sodium salt) in solution, wherein the composition has a bactericidal effect over a broad spectrum of microbes, has a pH of at least 9.5, and is packaged in a sterile, non-pyrogenic form.

Providing the claimed antiseptic compositions in a sterile, non-pyrogenic form is a significant feature. Because the claimed compositions are packaged in a sterile, non-pyrogenic form, they are safe for use in human health and veterinary applications and may be safe and biocompatible, at least in modest volumes, in a patient's bloodstream. Providing compositions packaged in a sterile, non-pyrogenic form typically requires special processing procedures for both packaging and solution components. These procedures are generally expensive and time consuming, and they may be subject to special regulations and approval by regulatory authorities. Care must be taken, for example, with regard to multiple potential sources for pyrogens, e.g., water used as a solvent or in processing, packaging components, raw materials, and equipment used. The time, effort and risk associated with providing compositions, such as the claimed antiseptic compositions, in a sterile, non-pyrogenic form are substantial.

Fahim discloses an antimicrobial **handwash** composition that may comprise tetra-sodium EDTA. The disclosure of Fahim suggests that the antimicrobial handwash compositions of Fahim are formulated and intended for use by employees in the food industry. The Examiner acknowledges that Fahim does not teach or suggest that the composition is packaged in a sterile, non-pyrogenic form. The exemplary compositions, formulation methodologies and animal testing protocols

described in Fahim do not disclose or suggest any sterility precautions or post-formulation sterilizing procedures. Appellants find no uses or proposed uses of the Fahim antimicrobial handwash compositions that would suggest providing the compositions of Fahim in a sterile, non-pyrogenic form would be necessary or advisable.

To remedy this deficiency of Fahim, the Examiner combines an isolated teaching from Wider with the handwash composition of Fahim. Applicants do not perceive any suggestion to combine the references in the manner proposed by the Examiner, or any motivation for doing so.

Wider discloses a fatty acid-based biocidal antimicrobial composition comprising an organic acid to maintain the composition at a pH below 5.0. The antimicrobial composition of Wider is intended for the treatment of microbial infections *of the body spaces and organs* of man or animals (*See, e.g.,* Col. 3, lines 59-65) and is administered as a liquid either orally or through a suitable delivery system, such as a catheter, an enema tube, needle or the like, or as a solid in tablet or encapsulated form. (*See, e.g.,* Col 4, lines 10-14.) Wider discloses an exemplary protocol for producing a composition that is sterile and pyrogen free (*See,* Example 1, Col. 7, lines 50-51) and discloses that peritoneal dialysis requires the use of sterile and pyrogen free fluids (*See*, Col. 6, lines 5-11). The compositions of Wider are disclosed as useful as an adjunct to peritoneal dialysis.

It is manifestly improper to piece together isolated teachings in the art in an attempt to meet the claimed subject matter. *In re Vaeck*, 947 F.2d 448, 20 USPQ2d 1438 (Fed. Cir. 1991) ("The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on Appellants' disclosure."). Here, the Examiner has done just this - improperly pieced together isolated teachings in the art without consideration for the invention as a whole, without consideration for whether one of ordinary skill in the art would be motivated to make the combination, and based on appellants' own disclosure.

Moreover, "it is the invention as a whole that must be considered in obviousness determinations. The invention as a whole embraces the structure, its properties and the problems it solves." *In re Wright*, 848 F.2d 1216 (Fed. Cir. 1988)." Accordingly, "casting an invention as a 'combination of old elements' leads

improperly to an analysis of the claimed invention by the parts, not by the whole." *Custom Accessories, Inc. v. Jeffery Allen Indus.*, 807 F. 2d 955 (Fed. Cir. 1987).

The claimed compositions are packaged in a sterile, non-pyrogenic form. Because the claimed compositions are packaged in a sterile, non-pyrogenic form, the claimed compositions are safe for use in human health and veterinary applications and may be safe and biocompatible, at least in modest volumes, in a patient's bloodstream. Thus, considering the claimed compositions as a whole, one skilled in the art would not modify the handwash of Fahim with the teachings of Wider to arrive at the claimed compositions. That is, one skilled in the art, aware of Wider's alleged teaching of antimicrobial compositions packaged in a sterile, pyrogen free form and designed for treatment of internal body spaces or organs, would not be motivated to modify a **handwash** composition to make it a sterile, pyrogen-free composition. There is simply no reason for one skilled in the art to package a handwash in a sterile, non-pyrogenic form because, for example, a handwash does not typically come into contact with a user in a manner where packaging in a sterile, non-pyrogenic form would be beneficial. A handwash composition is not intended for potential contact with a patient's bloodstream or to otherwise be possibly introduced into the patient's body. A handwash is simply meant to cleanse the skin.

However, the Examiner insists that one skilled in the art would be motivated to make the combination of Fahim and Wider in order to arrive at the presently claimed invention.

The alleged motivation to make this combination is that Wider allegedly teaches antimicrobial compositions that are packaged in a sterile and pyrogen free form and are used for eliminating infections from various surfaces, including the surface of the body. This is a mischaracterization of Wider and does not provide proper motivation to one skilled in the art to provide the antimicrobial handwash composition of Fahim in a sterile, non-pyrogenic form (see discussion, *supra*).

The Examiner's assertion that Wider teaches antimicrobial compositions for eliminating infection from the surface of the body is a mischaracterization because the applications of Wider are contemplated for contact with skin that is not normally exposed (i.e., broken, cut skin). As specifically disclosed in the passage beginning

at column 5, line 50, Wider teaches that the composition is for "internal spaces"[1] and expressly states:

> It is also contemplated that the present compositions be used for the elimination of microorganisms from exposed body tissues that ***normally are not exposed***, such as the skin and underlying structure exposed by trauma or incision for or during surgery, or because of the ***introduction of surgical instruments*** or other such devices, such as vascular catheters and the like. (Emphasis added).

This surgical application is the same application that the Examiner relies on (at column 6, line 53-55) to assert that Wider teaches antimicrobial compositions for eliminating infection from the surface of the body. Specifically, the application relied upon by the Examiner is a pre-surgical application of a composition. Thus, the application relied upon by the Examiner is for skin that is not normally exposed. One skilled in the art would not be motivated to modify a handwash based on the teachings of a composition that is for skin that is not normally exposed (i.e., broken, cut skin).

Moreover, Wider only recites specific applications of the composition wherein the composition should be in "sterile and pyrogen free" form. This application is for the treatment of "internal spaces." A specific application of the composition is as an adjunct to peritoneal dialysis where there is a risk of infection of the abdominal cavity. It is for this reason that Wider teaches at column 6, lines 5-11 (a passage relied on by the Examiner) that hypertonic dialysis fluid should be in "sterile and pyrogen free" form. Wider does not teach or suggest that other potential applications of the composition, such as an application that is not for the "internal spaces," should be in "sterile and pyrogen free" form. The Examiner cannot extrapolate such teachings from Wider. Statements of a prior art reference cannot be viewed in the abstract. Rather, they must be considered in the context of the teaching of the entire reference. See *In re Kotzab*, 208 F.2d 1352 (Fed. Cir. 2000). One skilled in the art reading Wider would understand that the composition would be in a sterile and pyrogen free form only because of the potential use on "internal spaces." That is, one skilled in the art would understand that Wider is not suggesting that a composition be placed in a sterile and pyrogen free form for other

[1] "The term 'internal spaces' is meant to include, for example, the thorax, abdomen, gastrointestinal tract, urinary bladder, vagina, nasal sinuses, external auditory canal, urethra, and the like." Column 5, lines 52-55.

(non "internal spaces") purposes. Thus, Wider does not teach or suggest the use of a composition in a "sterile and pyrogen free" form for anything but the treatment of internal spaces. Accordingly, Wider is an isolated teaching of a composition in a "sterile and pyrogen free" form that is not applicable to a handwash that would *not* be used in "internal spaces." And, one skilled in the art would not be motivated to modify a handwash based on the teachings of a composition used for the treatment of internal spaces.

Accordingly, appellants assert that 1) Wider does not teach or suggest applications for normal state skin surfaces and 2) Wider only teaches a "sterile and pyrogen free" form for uses on "internal spaces."

Fahim, on the other hand, does not teach or suggest the use of a composition for the treatment or potential treatment of internal spaces. Fahim is simply focused on an antimicrobial **handwash** composition. See, e.g., Abstract and Field of Invention ("the invention relates to liquid antimicrobial handwash compositions"). Needless to state, a handwash composition is specifically designed to treat just the skin surfaces. For example, as may be seen from Example 11, when the composition of Fahim is placed in the eye of a rabbit, ocular irritation in the form of corneal opacity and conjunctivitis occurred.

Thus, the attempt of the Examiner to piece together an isolated teaching from Wider with the teachings of Fahim is devoid of proper consideration of the claimed invention as a whole and is made without the required suggestion to combine the references.

As discussed above, one skilled in the art would not modify a **handwash** composition to make it a sterile, pyrogen-free composition. There is no motivation to make such a modification found in the art. It is completely foreign and unnecessary to package a handwash composition in a sterile, non-pyrogenic form. There is no reason for one skilled in the art to package a handwash in a sterile, non-pyrogenic form because, for example, a handwash does not typically come into contact with a user in a manner where packaging in a sterile, non-pyrogenic form would be beneficial. A handwash composition is not intended for potential contact with a patient's bloodstream or to otherwise be possibly introduced into the "internal spaces" of a patient's body. A handwash is simply meant to cleanse the skin.

Moreover, one skilled in the art would not be motivated by the teaching of a sterile, pyrogen-free composition for "internal spaces" or body tissues that are normally not exposed to modify a **handwash** composition. To then undergo the extra time and expense to package a handwash in a sterile, non-pyrogenic form would not only not be obvious, it would actually be contrary to the teachings of Wider, which teach that the sterile and pyrogen free form should be used in applications on "internal spaces."

A further reason why it is improper to attempt to combine the teachings of Wider with those of Fahim is that Wider specifically requires a pH range of about 1.0 to about 5.0, preferably from about 2.5 to about 4.0. Column 4, lines 7-9 and 35-36. This range is several orders of magnitude from the pH recited in the claims on appeal (pH of at least 9.5) and is also substantially different from the pH of Fahim, which discloses a broad pH range of 5.0 to 11.0, preferably 5.5 to 10.5, and more preferably 7.5 to 9.5.

In this respect, it has long been established that it is impermissible under 35 U.S.C. § 103(a) to pick and choose from a reference only so much as will support a given position to the exclusion of other parts necessary to a full appreciation of what the reference fairly suggests to one of ordinary skill in the art. See *In re Wesslau*, 353 F.2d 238 (CCPA 1965). Yet, the Examiner has relied upon Wider without a full appreciation of what Wider fairly suggests to one of ordinary skill in the art. One of ordinary skill in the art would not rely on a reference with the pH range of Wider (1.0 to 5.0, preferably 2.5 to 4.0) to modify Fahim (pH range of 5.0 to 11.0, preferably 7.5 to 9.5) to arrive at the claims on appeal, which recite that the antiseptic composition has a pH of at least 9.5.

Accordingly, it is improper to attempt to combine the teachings of Wider with those of Fahim in order to arrive at the claims on appeal.

At best, the Board could take the position that it would be obvious to try the combination of prior art documents in the manner hypothesized in the Official Action. However, "obvious to try" is not the standard under 35 U.S.C. §103 as has been held by numerous decisions such as *In re Goodwin*, 198 USPQ 1 (CCPA 1978) and *In re Geiger*, 2 USPQ2d 1276 (Fed. Cir. 1987). All of these decisions have been previously discussed and appellants again assert their applicability without going into detail. Yet further, the positions taken by the Examiner in attempting to piece

together disparate teachings in the prior art are contrary to long standing decisions such as *In re Mercier*, 515 F.2d 1161, 1166, 185 USPQ 774, 778 (CCPA 1975) where the court reversed a prior art rejection stating: "The relevant portions of a reference include not only those teachings which would suggest particular aspects of an invention to one having ordinary skill in the art, but also teachings which would lead such a person away from the claimed invention."

Accordingly, the rejection of claims 32, 34, 39, 41, 42, 45, 55, 57 and 60 must be withdrawn.

Claim 56

The patentability of claim 56 is argued separately. Claim 56 specifies a lock flush composition comprising at least one of tri- and tetra-sodium EDTA in solution at a concentration of at least 2.0% (w/v) and less than 15% (w/v), having a pH of at least 9.5, packaged in a sterile, non-pyrogenic form, wherein the lock flush composition is biocompatible for use in in-dwelling catheters, urinary catheters, nasal tubes and throat tubes.

Appellants' arguments presented above with respect to the patentability of claims 32, 34, 39, 41, 42, 45, 55, 57 and 60 are reiterated with respect to the rejection of claim 56. Additionally, appellants submit that the combination of Fahim and Wider would *not* result in appellants' claimed lock flush composition. There is no suggestion that any composition of Fahim, even if it were packaged in a sterile, non-pyrogenic form, would be biocompatible for use in in-dwelling access catheters, urinary catheters, nasal tubes and throat tubes, as specified in claim 56. In fact, as mentioned previously, it is abundantly clear that the composition of Fahim, even if packaged in a sterile, non-pyrogenic form, would ***not*** be biocompatible for use in in-dwelling access catheters, urinary catheters, nasal tubes and throat tubes. Needless to state, a handwash composition is specifically designed to treat just the skin surfaces. There is no credibility in the assertion that the handwash composition of Fahim would be biocompatible for use in in-dwelling access catheters, urinary catheters, nasal tubes, or throat tubes. For example, as may be seen from Example 11, when the composition of Fahim is placed in the eye of a rabbit, ocular irritation in the form of corneal opacity and conjunctivitis occurred.

Neither Fahim nor Wider makes any suggestion to combine the teachings as proposed by the Examiner, and Appellants find no motivation to make any such combination. Furthermore, even if the combination were made, the combination does not result in the lock flush composition specified in appellants' claim 56. This rejection must be withdrawn.

Claims 58 and 59

The patentability of claims 58 and 59 is argued separately. Claims 58 and 59 are dependent and specify that the EDTA salt (claim 58) or the combination of tri- and tetra-sodium EDTA (claim 59) provides at least 50% of a total antimicrobial activity of the composition.

Appellants arguments presented above with respect to the patentability of claims 32, 34, 39, 41, 42, 45, 55, 56, 57 and 60 are reiterated with respect to the rejection of claims 58 and 59. The Examiner asserts that because Fahim discloses the same sodium salts of EDTA as are used in appellants' claims, the Fahim composition should possess the claimed properties (*See,* final rejection, page 6). Appellants respectfully traverse this rejection and submit the Examiner has not established a *prima facie* case of obviousness.

Fahim teaches a composition comprising three primary antimicrobial components: triclosan, PCMX (4-chloro-3,5-dimethyl phenol) and glutaraldehyde. An EDTA salt is not a required component, as is evident from the description of the first embodiment on page 5. Fahim teaches that EDTA or an EDTA salt (preferably tetra-sodium) may be added to the combination as an enhancer and allows formulation of a composition having a reduced amount of PCMX, improving the fragrance of the composition. (*See, e.g.,* page 10, lines 26-31.) It is evident that Fahim relies on the three primary components (triclosan, PCMX and glutaraldehyde) for the antimicrobial activity of the composition. Accordingly, Fahim does *not* teach or suggest that the EDTA salt, provided as an optional component in the antimicrobial combination composition, provides at least 50% of a total antimicrobial activity of the composition. And, based on the well-known and potent antimicrobial properties of the three primary components, triclosan, PCMX and glutaraldehyde, and the relative amounts of these primary components in the combination, it is

apparent that EDTA salt would not provide at least 50% of the total antimicrobial activity of the Fahim composition.

Neither Fahim nor Wider makes any suggestion to combine the teachings as proposed by the Examiner, and Appellants find no motivation to make any such combination. Furthermore, even if the combination were made, the combination does not result in the compositions set out in appellants' claims 58 and 59. This rejection must be withdrawn.

Conclusion

Accordingly, appellants respectfully request that the rejection of claims 32, 34, 39, 41, 42, 45, and 55-60 under § 103(a) as being obvious over Fahim in view of Wider, be withdrawn.

2) § 103(a) – Fahim in view of Wider and further in view of Root et al.

Claim 47 stands rejected under 35 USC § 103(a) as allegedly being obvious over Fahim (WO 00/13656) in view of Wider (US 6,500,861) and further in view of Root et al. Claim 47 depends from any of claims 32, 56 or 57 and further recites that the composition is in a single-dosage vial. This rejection is respectfully traversed.

The teachings of Fahim and Wider are described above with respect to the previous rejection. Appellants arguments presented above with respect to the patentability of claims 32, 34, 39, 41, 42, 45, 55, 56, 57 and 60 are reiterated with respect to the rejection of claim 47.

The Examiner concedes that Fahim does not specifically teach the antimicrobial composition in a single-dosage vial and further relies on the disclosure of Root et al. to motivate one of ordinary skill in the art to employ the handwash composition of Fahim in a sterile condition in a single-dosage vial.

Root et al. discloses the use of a di-sodium EDTA solution for inhibiting bacterial infection in intravenous catheters. During testing of the catheter flush solutions, the catheter flush solutions were inoculated with bacteria, incubated, and then centrifuged in sterile Eppendorf tubes. (*See*, Root et al., page 1628, lines 18-21, cited by the Examiner.) Sterile polystyrene test tubes were also used in some of Root et al.'s experimental protocols. Root et al. does not, however, overcome the

deficiencies of the combination of Fahim and Wider with respect to appellants' claimed antiseptic composition provided in a sterile, non-pyrogenic form in a single dosage vial, as specified by claim 47.

It would be absurd, unnecessary and prohibitively expensive to package the handwash composition of Fahim in a sterile condition in a single-dosage vial. Appellants submit that one of ordinary skill in the art would *not* be motivated by Root et al.'s use of sterile test tubes in experimental protocols to package the antimicrobial handwash composition of Fahim in a sterile, non-pyrogenic form in a single-dosage vial.

As stated above, it is manifestly improper to piece together isolated teachings in the art in an attempt to meet the claimed subject matter. Thus, the attempt to rely on Root et al., which relates to a catheter flush solution, to further modify the handwash composition of Fahim is improper. Reliance on Root et al. to provide a teaching of providing or motivation to provide the handwash composition of Fahim in a sterile, non-pyrogenic form in a single dosage vial is unfounded, is far outside the realm of obviousness, and could only be justified by improper resort to appellants' own specification and claims.

Accordingly, the Examiner has not set forth a proper *prima facie* case of obviousness and appellants respectfully request that the rejection of claim 47 under § 103(a) as being obvious over Fahim in view of Wider and further in view of Root et al. be withdrawn.

3) § 103(a) – Fahim in view of Wider and further in view of Remington's Pharmaceutical Sciences

Claim 46 stands rejected under 35 USC § 103(a) as being obvious over Fahim (WO 00/13656) in view of Wider (US 6,500,861) and further in view of Remington's Pharmaceutical Sciences. Claim 46 depends from any of claims 32, 56 or 57 and further recites that the composition is in a pre-filled syringe. This rejection is respectfully traversed.

The teachings of Fahim and Wider are described above with respect to the previous rejections. Appellants' arguments presented above with respect to the patentability of claims 32, 34, 39, 41, 42, 45, 55, 56, 57 and 60 are reiterated with respect to the rejection of claim 46.

The Examiner concedes that Fahim does not specifically teach the antimicrobial composition in a pre-filled syringe and further relies on the disclosure of Remington's Pharmaceutical Sciences to lead one of ordinary skill in the art to employ the antimicrobial composition of Fahim in a sterile condition in a pre-filled syringe.

Remington's Pharmaceutical Sciences teaches sterile, pyrogen free sodium chloride solutions for injection and hypodermic syringes for use for injection of liquids. The sodium chloride solution is disclosed to be an electrolyte replenisher administered intravenously. Remington's Pharmaceutical Sciences does not, however, lead one of ordinary skill in the art to provide appellants' claimed compositions in a sterile, non-pyrogenic form in a pre-filled syringe.

It would be absurd, unnecessary and prohibitively expensive to package the handwash composition of Fahim in a sterile condition in a pre-filled syringe. One skilled in the art would not be motivated by the teaching of a sterile, pyrogen-free electrolyte replenisher to modify a handwash. A handwash is not intended for potential contact with a patient's bloodstream or to otherwise be possibly introduced into a patient's body. A handwash is simply meant to cleanse the skin. Thus, there is no reason for one skilled in the art to package a handwash in a sterile, non-pyrogenic form because, for example, a handwash does not typically come into contact with a user in a manner where packaging in a sterile, non-pyrogenic form would be beneficial. One skilled in the art would not be motivated by a teaching of a sterile, pyrogen-free electrolyte replenisher to then undergo the extra time and expense to package a handwash in a sterile, non-pyrogenic form.

As stated above, it is manifestly improper to piece together isolated teachings in the art in an attempt to meet the claimed subject matter. Reliance on Remington's Pharmaceutical Sciences to provide a teaching or motivation to provide the handwash composition of Fahim in a sterile, non-pyrogenic form in a pre-filled syringe is unfounded, is far outside the realm of obviousness, and could only be justified by improper resort to appellants' own specification and claims.

Accordingly, the Examiner has not set forth a proper *prima facie* case of obviousness and appellants respectfully request that the rejection of claim 46 under § 103(a) as being obvious over Fahim in view of Wider and further in view of Remington Pharmaceutical Sciences, be withdrawn.

4) - § 103(a) – Kurginski in view of Fahim and in view of Wider

Claims 32, 34, 37, 41, 42, 45, and 55-60 stand rejected under 35 USC §103(a) as allegedly being obvious over Kurginski (GB 1 279 148) in view of Fahim (WO 00/13656) and in view of Wider (US 6,500,861). Appellants submit that the Examiner has not established a *prima facie* case of obviousness and this rejection must therefore be withdrawn.

Claims 32, 34, 37, 41, 42, 45, 55, 57 and 60

Claims 32, 34, 37, 41, 42, 45, 55, 57 and 60 are argued as a group with respect to patentability in view of the final rejection. The recitations of these claims have been summarized in connection with the previous rejection(s) and the teachings of the Fahim and Wider references have been discussed. The significance of providing of the appellants' claimed compositions in a sterile, non-pyrogenic form has also been emphasized.

Kurginski discloses "a cleaning composition useful for releasing the particular soils that tend to accumulate in toilets and similar sanitary facilities." Kurginski, page 1, lines 12-15. The soils to be cleaned include the "hard, rock-like, white or nearly white deposit, which is some kind of **reaction product from urine**, **adherent fecal matter**, ... and **rust**." *See, e.g.,* Kurginski, page 1, lines 25-60. The toilet cleaning composition of Kurginski comprises a lower alkanol, an alkanolamine, a mixture of two or more different lower alkyl ether alcohols and a chelator. Tetra-sodium EDTA is disclosed as a potential chelator for use in the compositions. While the composition of Kurginski may comprise tetra-sodium EDTA, it is improper to treat the composition of Kurginski as simply a generic composition which comprises tetra-sodium EDTA. It is a toilet cleaning composition.

The Examiner concedes that Kurginski does not teach its composition packaged in a sterile, non-pyrogenic form. The Examiner asserts that "It would have been obvious to a person of ordinary skill in the art to employ the compositions comprising sodium salts of EDTA [Kurginski] as antimicrobial compositions, as Fahim teaches that the compositions comprising tetra-sodium EDTA can be used as antimicrobial compositions." (*See*, Final Office Action of February 24, 2006, page 9.) The Examiner posits that because the two compositions have one constituent in

common, each may be used in the intended applications of the other. Thus, the Examiner proposes that one of ordinary skill in the art would be motivated to use the toilet cleaning composition (Kurginski) as an antimicrobial handwash composition (Fahim).

The composition of Kurginski is not simply a generic composition comprising sodium salts of EDTA that can be used/modified as any other composition that also comprises sodium salts of EDTA. The composition of Kurginski is a **toilet cleanser**. To establish a prima facie case of obviousness, the Examiner must find a suggestion in the art to combine teachings, or a motivation for one of ordinary skill in the art to combine teachings. The identification of one common constituent in disparate combination compositions used for different applications provides neither the requisite suggestion or motivation. That is, the Examiner must assert motivation to rely on a toilet cleanser to modify a handwash - and not just rely on a mischaracterization of Kurginski as a generic composition that comprises sodium salts of EDTA to modify another generic composition comprising tetra-sodium EDTA. The Examiner has not asserted a proper motivation to rely on a toilet cleanser to modify a handwash.

It is evident that the Examiner has improperly pieced together isolated teachings in the art without consideration for the invention as a whole. One skilled in the art would not be motivated to use the **toilet cleanser** of Kurginski, which is designed to treat rock-like deposits derived from urine, fecal matter and rust, for cleaning **skin**.

There is no motivation to adapt a toilet cleanser in a manner to arrive at the presently claimed invention.

Furthermore, appellants' claims recite antiseptic compositions having a bactericidal effect over a broad spectrum of microbes. There is no indication in Kurginski that the composition of Kurginski, optionally containing tetra-sodium EDTA, has any antimicrobial properties. Kurginski teaches, in fact, that when desired, a germicide can be added to the toilet cleaning composition to disinfect or sterilize surfaces. (See, e.g., Col. 3, lines 74-79.)

Even if one skilled in the art would be motivated to employ the toilet cleaning compositions of Kurginski as an antimicrobial handwash, there is no suggestion or motivation, whatsoever, to package the composition of Kurginski in a sterile, non-

pyrogenic form. There is no suggestion made in Kurginski, Fahim or Wider to combine the elements of the various references in the manner proposed by the Examiner, and there is no motivation for doing do. It would be absurd, unnecessary and prohibitively expensive, and would serve no purpose, to package the toilet cleanser of Kurginski in a sterile, non-pyrogenic form.

As pointed out above, the question under 35 U.S.C. 103(a) is not whether the differences between the claimed invention and the prior art would have been obvious, but whether the claimed invention as a whole would have been obvious. *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 218 USPQ 871 (Fed. Cir. 1983); *Schenck v. Norton Corp.*, 713. F.2d 782, 218 USPQ 698 (Fed. Cir. 1983).

The attempt by the Examiner to piece together isolated teachings from Wider and Fahim to modify Kurginski in the manner proposed is devoid of proper consideration of the claimed invention as a whole and without proper consideration of the teachings of the prior art references as a whole. One skilled in the art would not be motivated to provide the **toilet cleanser** composition of Kurginski in a sterile, non-pyrogenic form.

There is no motivation to make such a modification found in the art. It is completely foreign and unnecessary to package a toilet cleanser composition in a sterile, non-pyrogenic form. There is no reason for one skilled in the art to package a toilet cleanser in a sterile, non-pyrogenic form because, for example, a toilet cleanser does not typically come into contact with a user, let alone in a manner where packaging in a sterile, non-pyrogenic form would be beneficial. A toilet cleanser composition is clearly not intended for potential contact with a patient's bloodstream or to otherwise be possibly introduced into the "internal spaces" of a patient's body. A toilet cleanser is simply meant to cleanse toilets. Thus, one skilled in the art would not be motivated by the teaching of a sterile, pyrogen-free composition to modify a **toilet cleanser** composition.

Additionally, the Examiner appears to rely on the combination of Fahim in view of Wider to attempt to remedy the substantial deficiencies of Kurginski, alleging that it would have been obvious to one skilled in the art to employ the composition of Fahim in a sterile, pyrogen-free condition because Wider allegedly teaches antimicrobial compositions packaged in a sterile, pyrogen-free form.

However, as addressed above, one skilled in the art would not have been motivated to incorporate the teachings of Wider into the composition of Fahim.

As discussed above, Fahim is focused on an antimicrobial handwash composition. To even attempt to combine this teaching with the toilet cleaning composition of Kurginski and the sterile, pyrogen-free composition of Wider would not be contemplated by those of ordinary skill in the art. Thus, there is no reason for one skilled in the art to package the toilet cleaning composition of Kurginski in a sterile, non-pyrogenic form even in view of the teachings of Fahim and Wider since there is no logical basis for packaging a toilet cleaning composition in a sterile, non-pyrogenic form.

Accordingly, the Examiner has not set forth a proper prima *facie case* of obviousness and this rejection must be withdrawn.

Claim 56

The patentability of claim 56 is argued separately. Claim 56 specifies a lock flush composition comprising at least one of tri- and tetra-sodium EDTA in solution at a concentration of at least 2.0% (w/v) and less than 15% (w/v), having a pH of at least 9.5, packaged in a sterile, non-pyrogenic form, wherein the lock flush composition is biocompatible for use in in-dwelling catheters, urinary catheters, nasal tubes and throat tubes.

Appellants' arguments presented above with respect to the patentability of claims 32, 34, 37, 41, 42, 45, 55, 57 and 60 are reiterated with respect to the rejection of claim 56. Additionally, appellants submit that the combination of Kurginski with Fahim and Wider would *not* result in appellants' claimed lock flush composition. There is no suggestion that any composition of Kurginski, even if it were packaged in a sterile, non-pyrogenic form, would be biocompatible for use in in-dwelling access catheters, urinary catheters, nasal tubes and throat tubes, as specified in claim 56. There is no credibility in the assertion that the composition of Kurginski, formulated to remove hard, rock-like, white or nearly white deposits, which are a reaction product from urine, adherent fecal matter and/or rust, would be biocompatible for use in in-dwelling access catheters, urinary catheters, nasal tubes and throat tubes.

Neither Kurginski nor Fahim nor Wider makes any suggestion to combine the teachings as proposed by the Examiner, and Appellants find no motivation to make any such combination. Furthermore, even if the combination were made, the combination does not result in the lock flush composition set out in appellants' claim 56. This rejection must be withdrawn.

Claims 58 and 59

The patentability of claims 58 and 59 is argued separately. Claims 58 and 59 are dependent and specify that the EDTA salt (claim 58) or the combination of tri- and tetra-sodium EDTA (claim 59) provides at least 50% of a total antimicrobial activity of the composition.

Appellants arguments presented above with respect to the patentability of claims 32, 34, 37, 41, 42, 45, 55, 56, 57 and 60 are reiterated with respect to the rejection of claims 58 and 59. The Examiner asserts that because Kurginski discloses the same sodium salts of EDTA as are used in appellants' claims, the Kurginski composition should possess the claimed properties (*See*, final rejection, page 10). Appellants respectfully traverse this rejection and submit that the Examiner has not established a *prima facie* case of obviousness.

Kurginski discloses a composition comprising a lower alkanol, an alkanolamine, a mixture of two or more different lower alkyl ether alcohols and a chelator. Tetra-sodium EDTA is disclosed as a potential chelator for use in the compositions. Indeed, Kurginski does not teach that EDTA salt alone has any antimicrobial properties and teaches that a germicide can be added to the composition to disinfect or sterilize the surfaces. *See*, Kurginski, page 3, lines 74-76.

Neither Kurginski nor Fahim nor Wider makes any suggestion to combine the teachings as proposed by the Examiner, and there is no motivation to make any such combination. Furthermore, even if the combination were made, the combination does not result in the appellants' claimed compositions, in which the EDTA salt provides at least 50% of a total antimicrobial activity of the composition. This rejection must be withdrawn.

Conclusion

Accordingly, appellants respectfully request that the rejection of claims 32, 34, 37, 41, 42, 45, and 55-60 under § 103(a) as being obvious over Kurginski in view of Fahim and in view of Wider, be withdrawn.

Conclusion

In view of the foregoing, further and favorable consideration of the pending claims in the form of a Notice of Allowance is respectfully requested.

Respectfully submitted,
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Table of Contents

VIII. CLAIMS APPENDIX

The Appealed Claims

1. – 31. (Canceled)

32. (Previously presented) An antiseptic composition comprising at least one salt of ethylene diamine tetraacetic acid (EDTA) in solution, wherein the at least one EDTA salt comprises at least one of tri-sodium and tetra-sodium EDTA at a concentration of at least 2.0% (w/v) and less than 15% (w/v), wherein the antiseptic composition has a bactericidal effect over a broad spectrum of microbes, wherein the antiseptic composition has a pH of at least 9.5, and wherein the antiseptic composition is packaged in a sterile, non-pyrogenic form.

33. (Canceled)

34. (Previously presented) A composition of either of claims 55 or 56, comprising tri-sodium and tetra-sodium EDTA.

35. – 36. (Canceled)

37. (Previously presented) A composition of any of claims 32, 56 or 57, wherein the solution comprises less than 10% (v/v) ethanol and water.

38. (Canceled)

39. (Previously presented) A composition of any of claims 32, 56 or 57, wherein the solution comprises saline.

40. (Canceled)

41. (Previously presented) A composition of any of claims 32, 55 or 57 formulated for topical application to surfaces and objects.

42. (Previously presented) A composition of any of claims 32, 55 or 57,

comprising tri- and tetra-sodium EDTA salts in an aqueous solution at a concentration of between 2.0% and 8.0% (w/v) EDTA salt(s).

43. - 44. (Canceled)

45. (Previously presented) A composition provided in a dry or partially hydrated formulation that, upon reconstitution with a solution, forms an antiseptic composition of any of claims 32, 56 or 57.

46. (Previously presented) A composition of any of claims 32, 56 or 57 in a pre-filled syringe.

47. (Previously presented) A composition of any of claims 32, 56 or 57 in a single-dosage vial.

48. – 54. (Canceled)

55. (Previously presented) An antiseptic composition comprising at least one salt of ethylene diamine tetraacetic acid (EDTA) in solution, wherein the at least one EDTA salt comprises at least one of tri-sodium and tetra-sodium EDTA at a concentration of at least 2.0% (w/v) and less than 15% (w/v), wherein the antiseptic composition has a bactericidal effect over a broad spectrum of microbes, wherein the antiseptic composition has a pH of at least 9.5, wherein the antiseptic composition is packaged in a sterile, non-pyrogenic form, wherein the solution is water, and wherein the antiseptic composition has an osmolarity of from 240-500 mOsM/Kg.

56. (Previously presented) A lock flush composition comprising at least one salt of ethylene diamine tetraacetic acid (EDTA) in solution, wherein the at least one EDTA salt comprises at least one of tri-sodium and tetra-sodium EDTA at a concentration of at least 2.0% (w/v) and less than 15% (w/v), wherein the lock flush composition has a pH of at least 9.5, wherein the lock flush composition is packaged in a sterile, non-pyrogenic form, and wherein the lock flush composition is

biocompatible for use in in-dwelling access catheters, urinary catheters, nasal tubes and throat tubes.

57. (Previously presented) An antiseptic composition comprising tri-sodium and tetra-sodium ethylene diamine tetraacetic acid (EDTA) in solution at a concentration sufficient to have antimicrobial activity, wherein the antiseptic composition has a bactericidal effect over a broad spectrum of microbes, wherein the antiseptic composition has a pH of at least 9.5, and wherein the antiseptic composition is packaged in a sterile, non-pyrogenic form.

58. (Previously presented) A composition of any of claims 32, 55 or 56, wherein the EDTA salt provides at least 50% of a total antimicrobial activity of the composition.

59. (Previously presented) A composition according to claim 57, wherein the combination of tri-sodium and tetra-sodium EDTA provides at least 50% of a total antimicrobial activity of the composition.

60. (Previously presented) A composition according to claim 57, wherein the concentration of tri-sodium and tetra-sodium EDTA in solution is at least 2.0% (w/v) and less then 15% (w/v).

IX. EVIDENCE APPENDIX

None

X. RELATED PROCEEDINGS APPENDIX

The Board is directed to an Appeal and associated Appeal Brief for U.S. Patent Application Serial No. 10/313,844, attached.